EFFECTS OF PROSTAGLANDIN I$_2$ AND E$_2$ ON
RENAL HEMODYNAMICS AND
FUNCTION AND RENIN RELEASE

MASAHITO IMANISHI, YOICHI ABE, TAKESHI OKAHARA,
TOKIITO YUKIMURA, KENJIRO YAMAMOTO

The effects of PGI$_2$ and PGE$_2$, given in the same doses were compared as to renal hemodynamics and functions and renin release. The same experimental conditions were used for both compounds and experiments were carried out in pentobarbital anesthetized dogs. Adrenergic influences were excluded by renal denervation. Given intrarenally at doses of 0.1 μg/min and 1 μg/min, PGE$_2$ caused significant increase in RBF, UF and UNaV, but had no effect on BP and GFR. Intrarenal infusion of PGI$_2$ at a rate of 1 μg/min resulted in a significant increase of RBF and in a marked fall of BP, but only little change in GFR, UF and UNaV. With a dose of 0.1 μg/min, the parameters remained the same. Intravenous infusion of PGI$_2$ (1 μg/min) caused a significant fall in BP with no change in the other parameters. Both PGI$_2$ and PGE$_2$ had a similar effect on intrarenal hemodynamics, i.e., caused a progressively greater proportional vasodilation from superficial to deep cortex. Given intrarenally in a dose of 1 μg/min, PGI$_2$ and PGE$_2$ increased renin release. But with a dose of 0.1 μg/min and 1 μg/min, i.v., renin secretion was not influenced. The effect of PGI$_2$ on systemic blood pressure was more potent than that of PGE$_2$, however, with regard to renal vasodilating action and tubular effects, PGE$_2$ was the more potent. Present data indicate that PGI$_2$ and PGE$_2$ stimulate renin secretion through a direct action on the juxtaglomerular cells.

Although physiological function of prostaglandins in the kidney is not clear, it has been considered that these prostanoic acids may contribute to the regulation of renal function through modification of renal hemodynamics and tubular effects.$^1$–$^3$ The principal intermediary of the renal prostaglandin system, prostaglandin E$_2$ (PGE$_2$), is a potent vasodilator and causes natriuresis$^4,5$ with a direct tubular action in dogs. Similar effects can be produced by arachidonic acid, the precursor of the renal prostaglandins$^6,7$

Prostaglandin I$_2$ (PGI$_2$), a potent vasodepressor prostaglandin in all species tested, is a product of prostaglandin endoperoxide metabolism in blood vessel microsomes$^8,9$ including those of the kidney. Infused into the renal artery of the dog, PGI$_2$ increased renal blood flow (RBF), urine flow and electrolytes excretion$^{10,11}$ PGI$_2$ is characterized by a marked dilation of renal vessels and a marked vasodepressor action in

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Prostaglandin E$_2$
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Renin release

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various anesthetized species, and is more potent than PGE₂. Thus, it has been suggested that PGI₂ may represent a circulating hormone exerting systemic biological effects, whereas primary prostaglandins may be less active metabolites.

In a variety of situations it was shown that prostaglandins participate in the regulation of renin release. We have previously reported that an intrarenal arterial infusion of PGE₂ in a low dose did not affect the renin release. However, Bolger et al. found that an infusion of PGE₂ into the canine renal artery did release renin while PGI₂ did not, whereas Hashimoto and Gerber et al. reported that PGE₂ and PGI₂ were equipotent in their capacity to release renin in the dog.

Using the same dose of PGI₂ and PGE₂ and the same experimental conditions we carried out studies to obtain more detail information about the role of these prostaglandins with regard to the regulation of renal hemodynamics and their influence on renin release.

MATERIALS AND METHODS

Adult mongrel dogs of either sex weighing 14–16 kg, were anesthetized with sodium pentobarbital (30 mg/kg, i.v.) and mechanically ventilated. The left kidney was exposed through a retroperitoneal flank incision, and all visible nerve fibers around the left renal artery and hilus were cut off. The left renal blood flow (RBF) was measured by an electromagnetic flow meter (Nihon-Koden, MF-25). Systemic blood pressure was measured from the left femoral artery which had been cannulated. A No. 23 gauge hooked needle attached to a polyethylene catheter was introduced into the left renal artery proximal to the flow probe and was used for the intrarenal infusion of saline and drug solutions at a rate of 0.5 ml/min. Another catheter was inserted into the right brachial vein to infuse saline at a rate of 3.5 ml/min. For the measurement of glomerular filtration rate (GFR) a priming dose of creatinine (100 mg/kg) was given into the right brachial vein, followed by a continuous infusion at a rate of 50 mg/kg/hr to maintain a constant blood level of creatinine. A polyethylene catheter was introduced into the left ureter for urine collection.

After completion of surgery, the dog was left for 60–90 min to allow for stabilization of RBF and urine flow, after which urine was collected during 3 consecutive 10-min control clearance periods. At the midpoint of each period, systemic arterial and renal venous blood samples were collected from the right brachial artery and from the left renal vein via a catheter introduced through the left spermatic or ovarian vein. These blood and urine samples were used for renin, creatinine and electrolytes estimation. After a control period, PGI₂ or PGE₂ was infused into the left renal artery or right brachial vein for 45 min (PG infusion periods), and then saline was infused for 30 min, as a recovery period. During this time, urine and blood samples were collected in the same manner as in the control period.

Procedures were as follows:
1. In 11 dogs, PGI₂ was infused into the renal artery at rates of 0.1 μg/min (n = 5) and 1.0 μg/min (n = 6).
2. In 6 dogs, PGI₂ was infused into the right brachial vein in a dose of 1 μg/min.
3. In 13 dogs, PGE₂ was infused into the renal artery at rates of 0.1 μg/min (n = 6) and 1.0 μg/min (n = 7).
4. In 10 dogs, intrarenal distribution of blood flow was examined after administration of PGI₂ (n = 5) and PGE₂ (n = 5) in a dose of 1 μg/min. The first microsphere injection was given during the control period and the second was given 15 min after the infusion of PGI₂ or PGE₂.

PGE₂ (The Upjohn Co.) was dissolved in ethanol (1 mg/ml) and the diluted with saline (0.2–2.0 μg/ml). The sodium salt of PGI₂ (kindly provided by Dr. B.A. Schölkens, Hoechst AG) was infused immediately after the dilution of stock solution (Tris buffer pH 9.5).

Analytical procedures

Glomerular filtration rate (GFR) was estimated by the creatinine clearance test. Sodium and potassium in plasma and urine were analyzed by a flame photometer (Hitachi 205D). Osmolality of arterial plasma and urine (Posm, Uosm) were measured by a Fiske osmometer (Fiske Associates, Inc., U.S.A.). Plasma renin activity (PRA) was determined by radioimmunoassay of angiotensin I and expressed as ng angiotensin I/ml·hr. The renin secretion rate (RSR) was calculated as the product of renin plasma flow and of the difference between renal venous PRA and arterial PRA and was expressed as ng angiotensin I per gram kidney/min.

Distribution of cortical blood flow was determined with radioactive microspheres (3M Company, St. Paul, Minn., U.S.A.) by the tech-
### TABLE I  EFFECTS OF INTRARENAL PGI$_2$ INFUSION ON RENAL FUNCTION AND PLASMA RENIN ACTIVITY

<table>
<thead>
<tr>
<th></th>
<th>Blood Pressure</th>
<th>Renal Blood Flow</th>
<th>Glomerular Filtration Rate</th>
<th>Urine Flow</th>
<th>Urinary Excretion Na</th>
<th>Urinary Excretion K</th>
<th>Plasma Renin Activity Artery</th>
<th>Plasma Renin Activity Vein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mmHg</td>
<td>mlg./min</td>
<td>mlg./min</td>
<td>µl/g-min</td>
<td>µEq/g-min</td>
<td>µEq/g-min</td>
<td>ng/mL/hr</td>
<td>ng/mL/hr</td>
</tr>
<tr>
<td>Control 1</td>
<td>121 ± 12</td>
<td>3.82 ± 0.57</td>
<td>0.71 ± 0.04</td>
<td>19.9 ± 4.7</td>
<td>3.85 ± 1.06</td>
<td>0.53 ± 0.11</td>
<td>5.1 ± 1.2</td>
<td>6.7 ± 2.8</td>
</tr>
<tr>
<td>2</td>
<td>121 ± 12</td>
<td>3.82 ± 0.57</td>
<td>0.71 ± 0.05</td>
<td>23.1 ± 5.3</td>
<td>4.73 ± 1.16</td>
<td>0.62 ± 0.11</td>
<td>6.2 ± 2.3</td>
<td>6.7 ± 2.5</td>
</tr>
<tr>
<td>Intrarenal infusion of PGI$_2$ at a rate of 0.1 µg/min</td>
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</tr>
<tr>
<td>10 min</td>
<td>120 ± 12</td>
<td>3.72 ± 0.71</td>
<td>0.68 ± 0.07</td>
<td>24.9 ± 6.6</td>
<td>4.72 ± 1.53</td>
<td>0.60 ± 0.13</td>
<td>5.8 ± 2.2</td>
<td>6.7 ± 2.6</td>
</tr>
<tr>
<td>30 min</td>
<td>120 ± 11</td>
<td>3.58 ± 0.62</td>
<td>0.65 ± 0.07</td>
<td>29.6 ± 8.3</td>
<td>4.76 ± 1.95</td>
<td>0.56 ± 0.16</td>
<td>6.3 ± 1.7</td>
<td>7.3 ± 2.3</td>
</tr>
<tr>
<td>Control 1</td>
<td>123 ± 8</td>
<td>3.09 ± 0.45</td>
<td>0.81 ± 0.07</td>
<td>14.9 ± 2.7</td>
<td>2.48 ± 0.42</td>
<td>0.35 ± 0.07</td>
<td>3.6 ± 0.7</td>
<td>4.4 ± 0.7</td>
</tr>
<tr>
<td>2</td>
<td>124 ± 7</td>
<td>3.14 ± 0.44</td>
<td>0.79 ± 0.07</td>
<td>15.8 ± 2.4</td>
<td>2.85 ± 0.47</td>
<td>0.41 ± 0.08</td>
<td>3.8 ± 0.9</td>
<td>4.8 ± 0.9</td>
</tr>
<tr>
<td>Intrarenal infusion of PGI$_2$ at a rate of 1 µg/min</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>10 min</td>
<td>112 ± 7**</td>
<td>4.76 ± 0.68**</td>
<td>0.81 ± 0.06</td>
<td>19.1 ± 4.2</td>
<td>2.52 ± 0.59</td>
<td>0.46 ± 0.08</td>
<td>9.1 ± 2.8</td>
<td>13.7 ± 5.2**</td>
</tr>
<tr>
<td>30 min</td>
<td>109 ± 6**</td>
<td>4.83 ± 0.75**</td>
<td>0.82 ± 0.06</td>
<td>20.6 ± 3.9</td>
<td>2.43 ± 0.48</td>
<td>0.47 ± 0.07</td>
<td>9.2 ± 3.0**</td>
<td>12.1 ± 3.0**</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.E.
*: P < 0.05, **: P < 0.01

### TABLE II  EFFECTS OF INTRAVENOUS INFUSION OF PGI$_2$ ON RENAL FUNCTION AND PLASMA RENIN ACTIVITY

<table>
<thead>
<tr>
<th></th>
<th>Blood Pressure</th>
<th>Renal Blood Flow</th>
<th>Glomerular Filtration Rate</th>
<th>Urine Flow</th>
<th>Urinary Excretion Na</th>
<th>Urinary Excretion K</th>
<th>Plasma Renin Activity Artery</th>
<th>Plasma Renin Activity Vein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mmHg</td>
<td>mlg./min</td>
<td>mlg./min</td>
<td>µl/g-min</td>
<td>µEq/g-min</td>
<td>µEq/g-min</td>
<td>ng/mL/hr</td>
<td>ng/mL/hr</td>
</tr>
<tr>
<td>Control 1</td>
<td>124 ± 9</td>
<td>3.18 ± 0.49</td>
<td>0.83 ± 0.17</td>
<td>30.1 ± 9.3</td>
<td>4.98 ± 2.08</td>
<td>0.84 ± 0.19</td>
<td>7.6 ± 1.9</td>
<td>7.7 ± 2.8</td>
</tr>
<tr>
<td>2</td>
<td>124 ± 9</td>
<td>3.20 ± 0.51</td>
<td>0.82 ± 0.16</td>
<td>31.5 ± 9.9</td>
<td>5.43 ± 2.35</td>
<td>0.84 ± 0.19</td>
<td>8.2 ± 1.9</td>
<td>8.0 ± 2.6</td>
</tr>
<tr>
<td>Intravenous infusion of PGI$_2$ at a rate of 1 µg/min</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>10 min</td>
<td>107 ± 10**</td>
<td>3.36 ± 0.35</td>
<td>0.92 ± 0.23</td>
<td>20.5 ± 3.3</td>
<td>2.98 ± 0.95</td>
<td>0.72 ± 0.26</td>
<td>8.1 ± 2.4</td>
<td>8.7 ± 2.5</td>
</tr>
<tr>
<td>30 min</td>
<td>106 ± 8**</td>
<td>3.54 ± 0.53</td>
<td>0.87 ± 0.17</td>
<td>22.3 ± 3.5</td>
<td>4.00 ± 1.19</td>
<td>0.78 ± 0.25</td>
<td>7.3 ± 2.1</td>
<td>7.7 ± 2.3</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.E. (n = 6).
**: P < 0.01
effect on renal hemodynamics, urine flow, urinary excretion of sodium and potassium, and PRA (Table I). When 1.0 μg/min was given, systemic arterial pressure decreased from 124 ± 7 to 112 ± 7 mmHg, but RBF increased from 3.14 ± 0.44 to 4.76 ± 0.68 ml/g-min and RSR also increased (Table I, Fig. 1). The responses in RBF and blood pressure reached their maximum about 10 min after the start of infusion and remained at the level for consecutive periods. RSR rose during the first 10 min of the infusion and was maintained at high levels in consecutive periods (Fig. 2). Although there were significant changes in renal hemodynamics and RSR, urine flow and urinary excretion of sodium and potassium changed little and GFR was fairly constant.

2. Effects of intravenous infusion of PGI₂

Intravenous infusion of PGI₂ at a rate of 1 μg/min infusion induced a significant fall of systemic arterial blood pressure from 124 ± 9 to 107 ± 10 mmHg, but RBF, GFR and UF were not influenced. Renal venous PRA and RSR were not changed even though there was a significant fall of systemic arterial blood pressure (Table II).

3. Effects of intrarenal infusion of PGE₂

PGE₂ infusion at a rate of 0.1 μg/min resulted in a significant increase in RBF, urine flow and urinary excretion of sodium and potassium without any change in systemic blood pressure and GFR. These responses reached a maximum within 10 min after the start of infusion and such high levels were maintained for consecutive periods. Although there were significant changes in renal hemodynamics and urine flow, PRA and RSR remained unchanged (Table III, Fig. 2). The infusion of PGE₂ at a rate of 1.0 μg/min produced renal hemodynamic and diuretic responses qualitatively and quantitatively similar to those observed with 0.1 μg/min with maximal responses within 10 min. Whereas, osmolar clearance was increased and production of free water was decreased with a dose of 1 μg/min. Renal venous PRA and RSR rose during the first 10 min of the infusion and were maintained at high levels in the consecutive periods (Table III, Figs. 1, 2).

4. Effects of PGI₂ and PGE₂ on intrarenal distribution of blood flow

Percent distribution of a total renal blood

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nique described in a previous paper.¹⁸ The renal cortex was cut parallel to the surface into four zones of equal thickness. Four cortex zones were analyzed for individual isotope counts, and the perfusion rate of each zone was calculated. The volume of each cortex zone was approximated by calculations based on the formula for an ellipsoid. The volume of the individual cortex zone, expressed as percent of total renal volume, was for zone 1; 27.0, zone 2; 21.9, zone 3; 17.3 and zone 4; 12.2.

The values presented in this paper are means ± S.E. Statistical significance was evaluated by means of Student’s paired- and non-paired-t test.

RESULTS

1. Effects of intrarenal infusion of PGI₂

PGI₂ infusion at a rate of 0.1 μg/min had no

Fig.1. Effects of PGI₂ and PGE₂ on arterial blood pressure (BP) and renal blood flow (RBF). (A): intrarenal arterial infusion at a rate of 0.1 μg/min. PGI₂ infusion affected neither BP nor RBF, but PGE₂ increased RBF without any change in BP. (B): intrarenal arterial infusion at a rate of 1 μg/min. PGI₂ infusion resulted in a fall of BP and an increase of RBF, whereas PGE₂ showed a pattern similar to (A). i.r.a.: intrarenal arterial infusion.
### TABLE III EFFECTS OF INTRARENAL PGE\textsubscript{2} INFUSION ON RENAL FUNCTION AND PLASMA RENIN ACTIVITY

<table>
<thead>
<tr>
<th>Blood Pressure (mmHg)</th>
<th>Renal Blood Flow Rate (ml/min)</th>
<th>Glomerular Filtration Rate (ml/min)</th>
<th>Urine Flow (ml/hr)</th>
<th>Urinary Excretion (µEq/min)</th>
<th>Osmolar Clearance (µEq/min)</th>
<th>Free Water Reabsorption Rate (µl/min)</th>
<th>Plasma Renin Activity (ng/ml/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control 1</td>
<td>116 ± 7</td>
<td>3.21 ± 0.46</td>
<td>0.66 ± 0.04</td>
<td>17.5 ± 4</td>
<td>3.41 ± 1.01</td>
<td>0.49 ± 0.09</td>
<td>35.9 ± 7.7</td>
</tr>
<tr>
<td>2</td>
<td>115 ± 7</td>
<td>3.51 ± 0.54</td>
<td>0.65 ± 0.04</td>
<td>19.6 ± 5</td>
<td>3.85 ± 1.22</td>
<td>0.56 ± 0.10</td>
<td>40.3 ± 9.6</td>
</tr>
<tr>
<td><strong>Intrarenal infusion of PGE\textsubscript{2} at a rate of 0.1 µg/min</strong></td>
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</tr>
<tr>
<td>10 min</td>
<td>114 ± 7</td>
<td>4.97 ± 0.59**</td>
<td>0.72 ± 0.07</td>
<td>48.2 ± 14.0*</td>
<td>6.77 ± 2.10*</td>
<td>0.67 ± 0.16</td>
<td>67.4 ± 20.9*</td>
</tr>
<tr>
<td>30 min</td>
<td>115 ± 7</td>
<td>4.63 ± 0.54**</td>
<td>0.72 ± 0.08</td>
<td>45.8 ± 11.3**</td>
<td>6.89 ± 1.79**</td>
<td>0.69 ± 0.14**</td>
<td>51.4 ± 12.1*</td>
</tr>
<tr>
<td>Control 1</td>
<td>118 ± 5</td>
<td>3.20 ± 0.30</td>
<td>0.85 ± 0.10</td>
<td>40.6 ± 7.2</td>
<td>5.34 ± 0.83</td>
<td>0.77 ± 0.15</td>
<td>43.9 ± 3.6</td>
</tr>
<tr>
<td>2</td>
<td>119 ± 5</td>
<td>3.20 ± 0.27</td>
<td>0.92 ± 0.11</td>
<td>47.7 ± 8.0</td>
<td>6.28 ± 1.17</td>
<td>0.80 ± 0.16</td>
<td>50.2 ± 5.6</td>
</tr>
<tr>
<td><strong>Intrarenal infusion of PGE\textsubscript{2} at a rate of 1 µg/min</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>10 min</td>
<td>118 ± 5</td>
<td>4.59 ± 0.44**</td>
<td>1.01 ± 0.07</td>
<td>107.2 ± 17.3**</td>
<td>11.90 ± 2.36**</td>
<td>1.23 ± 0.20*</td>
<td>75.7 ± 6.5**</td>
</tr>
<tr>
<td>30 min</td>
<td>118 ± 4</td>
<td>4.23 ± 0.45**</td>
<td>0.99 ± 0.13</td>
<td>94.6 ± 15.1**</td>
<td>10.20 ± 2.13*</td>
<td>1.20 ± 0.17*</td>
<td>77.9 ± 10.8**</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.E.  *: P < 0.05, **: P < 0.01

**DISCUSSION**

The present study demonstrated that intrarenal arterial infusion of PGE\textsubscript{2} at rates of 0.1 µg/min and 1.0 µg/min resulted in an increase in glomerular filtration rate and renal blood flow in the present study. Intrarenal arterial infusion of PGE\textsubscript{2} at a dose of 0.1 µg/min to each zone before and during PGE\textsubscript{2} and PGF\textsubscript{2} at rates of 0.1 µg/min and 1.0 µg/min increased the mean renal blood flow by 25% and 35%, respectively. This mode of expression incorporates the volume flow redistribution from the outer cortex to the inner cortex. Thus, the zonal response pattern was not uniform among zones, but was characterized by a progressively proportional increase in flow from the superficial to the deep cortex.

**Fig. 2. Renin secretion rate during renal arterial infusion of PGF2\textsubscript{2} and PGE\textsubscript{2}.** With a dose of 0.1 µg/min, renin secretion rate was significantly increased by both PGF\textsubscript{2} and PGE\textsubscript{2}. In a dose of 1.0 µg/min, renin secretion rate was significantly increased by PGF\textsubscript{2} and PGE\textsubscript{2}. In a dose of 0.1 µg/min, neither PGF\textsubscript{2} nor PGE\textsubscript{2} had any influence. I.R.A.: intrarenal arterial infusion.
Fig. 3. Effects of PGI₂ and PGE₂ in a dose of 1 μg/min, i.r.a. on renal blood flow (left panel), and on percent distribution of each cortex zone (right panel). Both prostaglandins increased the perfusion of each zone, and showed the same distribution pattern of renal cortical blood flow. The increasing rates in blood flow to the inner cortex were greater than those to the outer cortex. i.r.a.: intrarenal arterial infusion.

RBF with no change in the systemic arterial pressure. There was no qualitative and quantitative difference between the two doses. On the other hand, an intrarenal arterial infusion of PGI₂ at a rate of 0.1 μg/min had no effect on the renal hemodynamics and urine flow. 1.0 μg/min of PGI₂ showed a significant increase in RBF with a marked fall in systemic arterial pressure.

An intrarenal infusion of PGI₂ but not PGE₂ in a dose of 1.0 μg/min induced a significant fall of systemic blood pressure. PGI₂ undergoes little metabolism in the lung and kidney, and enough renal escapes to cause systemic effects. This is consistent with the observation made earlier by Gerkens et al.²⁰ that the vasodepressor response of PGI₂ in the dog is not diminished by passage through the lung, in contrast to a dramatic reduction, about 98%, in the vasodepressor effect of PGE₂. Other workers have also documented the renal vasodilation by PGE₂ and PGI₂.¹⁰,¹⁶,²¹ Our present study clearly showed that the vasodilating action of PGE₂ in a dose of 0.1 μg/min and PGI₂ at 1 μg/min was equipotent. This clearly indicates that the infusion of PGI₂ at a 10-fold higher rate produced a change in renal blood flow similar to the effect elicited by PGE₂. The effect of PGI₂ on systemic blood pressure was more potent than that of PGE₂, but regarding renal vasodilating action of PGE₂ was the more effective. Similar results were obtained by Hashimoto.¹¹

As shown in Fig. 3, PGI₂ and PGE₂ had the same pattern of distribution of renal cortical blood flow and the increases in blood flow to the inner cortex were greater than those to the outer cortex. An intrarenal infusion of arachidonic acid was found to induce the same changes in flow distribution pattern while indomethacin produced inverse changes.²² Other vasodilators: acetylcholine and bradykinin also increased the flow rate in all zones, the increase in inner cortex being greater than in outer cortex.¹⁹ Thus, PGI₂ had no specific effect on intrarenal hemodynamics. Since PGI₂ is synthesized from the prostaglandin endoperoxides by blood vessel microsomes including those in the kidney, escapes metabolism by the lung and possesses a potent vasodepressor action, it has been considered that this prostaglandin may function as a circulating vasodepressor hormone and as a regulator of renal hemodynamics.²³ However, it should be noted that PGI₂ exhibited no superior potency over PGE₂ regarding the effect on renal hemodynamics.

PGE₂ infusions in doses of 0.1 μg/min and 1.0 μg/min remarkably increased UF, U₅₁₀V and UᵥV with no change in GFR. In particular
PGE₂ 1 µg/min, i.r.a. infusion accelerated Cosm and suppressed free water production. This suppression indicates the inhibition of sodium and chloride transport in the ascending loop of Henle. On the contrary, PGI₂ had no effect on UF and its composition and the GFR remained unchanged. Bolger et al.ⁱ⁰ reported that an intrarenal infusion of PGI₂ in the dog produced changes in urine flow and composition which were qualitatively identical to those produced by PGE₂. On the other hand, Baer et al.⁳¹ reported that PGI₂ did not alter urine flow and composition in the rat. Although our findings did not elucidate the differences in the mechanisms between PGI₂ and PGE₂, they do indicate that PGI₂ probably does not act directly on the tubules.

There is evidence that prostaglandins play an important role in renal renin release⁷,¹³,²⁴,²⁵ Enhanced prostaglandin production by intrarenal infusion of arachidonic acid stimulates renin release, and inhibition of prostaglandin synthesis by indomethacin decreases renin release. Renal cortical microsomes produce mainly PGE₂, PGF₂α and PGI₂ from arachidonic acid. Among renal prostaglandins, PGE₂ and PGI₂ are the most likely candidates. However, the question remains as to which renal cortical prostaglandin mediates renin release. Vander²⁶ and our own group¹⁶ reported that infusion of PGE₂ or PGI₁ into the renal artery did not affect the renin release. Bolger et al.¹⁰ demonstrated that PGE₂ increased renin secretion in the dog but that PGI₂ was inactive. On the contrary, Gerber et al.¹³ found PGE₂ and PGI₂ to be equipotent in stimulating renin release. Hashimoto¹¹ also reported that both PGI₂ and PGE₂ caused significant increases in renal venous PRA.

Our present experiment demonstrated that the intrarenal infusion of PGE₂ at a rate of 0.1 µg/min did not affect renin secretion, but that PGE₂ in a dose of 1.0 µg/min produced a significant increase in renin release. Since there was a diuresis and also an increase in RBF during the infusion of PGE₂, the increase in renin secretion may be due to its diuretic action and renal vasodilation. Changes in renal hemodynamics and in urine output were identical with the dose of 0.1 µg/min and 1.0 µg/min. Thus, the increase in renin secretion caused by PGE₂ might depend on a direct action on the juxtaglomerular cells, but probably not via macroca densa cells or baroreceptors.

In the case of intrarenal arterial infusion of PGI₂, renin secretion was increased significantly with a dose of 1.0 µg/min but not with a dose of 0.1 µg/min, as was the case with PGE₂. The increase of renin release with PGI₂ may thus be due to a fall in systemic arterial pressure, however, the intravenous infusion of PGI₂ in a dose of 1.0 µg/min caused relatively greater falls in blood pressure, compared to the level produced by intrarenal infusion. The rate of renin secretion was not influenced. On the basis of these findings, it was considered that both PGI₂ and PGE₂ stimulate renin secretion through a direct action on the juxtaglomerular cells.

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